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(54) PATCH AND CONTROLLER FOR THE PHOTODYNAMIC THERAPY OF A DERMAL LESION

PFLASTER UND STEUEREINRICHTUNG FÜR PHOTODYNAMISCHE THERAPIE VON DERMALEN VERLETZUNGEN

PATCH ET SYSTEME DE CONTROLE DE TRAITEMENT PHOTODYNAMIQUE D'UNE LESION DERMIQUE

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Description

[0001] This invention relates generally to a patch, controller and method for the photodynamic therapy (PDT) of a dermal lesion such as actinic keratosis, basal carcinoma and psoriasis. More particularly, this invention relates to a portable combination controller and patch and method for applying photodynamic therapy (PDT) to a dermal lesion using a light or photoactivated photopharmaceutical.

[0002] Bodies, sheet or layer forms, of hydrogel or hydrogel materials, particularly transparent hydrogel or hydrogel materials, are well known in the medical field and may comprise, for example, a polyvinyl alcohol with a water matrix. Some of these transparent hydrogel or hydrogel materials are castable and can be cast into intimate contact with other devices. They have been widely adapted to such applications as diagnostic electrodes (for EKG), wound care dressings, and transdermal delivery devices for systemic delivery of pharmaceutical agents. The biocompatability of this class of materials is well established for extended contact with dermal structures.

[0003] Much of the prior art in medical applications for hydrogel or hydrogel materials relates to devices and methods for electrical conductivity enhancement. Critical in using hydrogel in many medical applications, such as an electrical interface, is the ability of the hydrogel to form intimate physical contact with skin or dermal structures. U.S. Patent No. 5,143,071 issued to Keusch *et al.* on September 1, 1992, has an extensive list and description of prior art hydrogels suitable for this purposes.

[0004] A concurrent body of prior art embraces hydrogels or hydrocolloids, as wound dressings and dressings impregnated with pharmaceutical compounds. Representative of this prior art is U.S. Patent No. 5,156,601 to Lorenze *et al.* Further, the work of Gombotz *et al., Proc. Intl. Symp. Cont. Rel. Bioact. Mtl.,* Vol. 19, 1992, describes the rapid release of complex compounds from hydrogels to skin or dermal structures.

[0005] U.S. Patent No. 5,079,262 issued to Kennedy *et al.* discloses a method of detection and treatment of malignant and non-malignant lesions utilizing 5-aminolevulinic acid ("ALA"). ALA is administered to a patient in an amount sufficient to induce biosynthesis of protoporphyrin IX in the lesions, and is followed by exposure of the treated lesions to a photoactivating light in the range of 350-640 nm. ALA is taught to be administered to a patient orally, topically or by injection.

[0006] None of the prior art references teach or suggest using hydrogel as an optical, chemical and fluidic coupling agent for light in the photodynamic therapy of dermal lesions. Since its first reported clinical use at the turn of the century, photodynamic therapy has been accomplished using light projected to the dermal treatment site from sources at some distance from the site. Modern photodynamic therapy (from 1978 onward) has developed light delivery protocols using artificial sources such as tungsten halogen or xenon arc lamps with wavelength filtration to activate photopharmaceuticals. All of the above light sources have been used in projective, field-illuminating devices that flood the target treatment field or site in the treatment of superficial cutaneous lesions with light containing a wavelength designed to activate the photopharmaceutical. These references generally teach that the dosimetry of applied photodynamic therapy can be controlled and varied by varying the intensity and/or duration of the photoactivating light applied to a photopharmaceutical performing photodynamic therapy.

[0007] In the case of the tungsten and xenon-arc sources, extensive filtration of the available light flux is essential to restrict the delivered energy to appropriate wavelengths that photoactivate the photopharmaceutical in the target dermal structures. Colored glass or interference filters used with these sources transmit some portion of unwanted wavelengths, notably in the infrared region, and can cause thermal effects that may mask the effect of photoactivity with an undesirable heating effect that also preferentially damages malignant tissue. High-power surgical lasers, even when de-focussed, also can induce undesirable thermal effects. The work of Svaasland, *Photochem/Photobiol.*, 1985, measured this effect and its impact on PDT protocols.

[0008] Dosimetry of delivered photodynamically effective light to a dermal treatment site is extremely difficult using current projective optics. Mathematical modeling of skin optics has been a slow and difficult process. Recent publications by Van Gemert *et al.*, *IEEE Trans. Biomed. Eng.,* Vol. 36; 12, 1989, critically reviewed the prior work and presents a 4-layer model of light-dermal tissue interaction. Van Gemert *et al.* elaborates on the advantages and effectiveness of the diffusion model of light transport in tissue, which depends upon the efficient coupling of the externally applied light to the target tissue. A later publication by R. Rox Anderson, *Optics of the Skin, Clinical Photomedicine,* Dekker Publication, 1993, reviews the two basic processes which govern the optics or behavior of light in skin, namely, light absorption and light scattering.

[0009] DE-A-38 03 763 discloses the use of a monocrystal as coupling means between the source of light and the biological matter to be irradiated. In "Photophysical characterization of hermatoporphyrin incorporated within collagen gels", *J. Photochem. Photobiol. B: Biol,* 22 (1994), 45-50, gel-embedded sensitizers are used for photodynamic treatment of cancer.

[0010] An apparatus comprising the features of the preamble of claim 1 of this application is described in US 5,057,104, relating to a method for treating cutaneous vascular lesions.

Summary of the Invention

[0011] It has been found that an efficient and practical means of establishing the diffusion conditions of light

transport is to provide a transparent coupling means that is in intimate contact with the skin containing dermal lesions on one surface and with the light source on its opposite surface. Under these conditions, reflective losses are reduced, and delivered optical energy is much more efficiently transmitted into the target region.

[0012] The stratum corneum present at a dermal treatment site on the skin of a person is a formidable barrier to transport (transmission, penetrability or permeability) of light into the deeper structures of the skin where dermal lesions typically reside, in whole or in part. The layered plate-light corneocytes comprising the stratum corneum constitute an efficient reflective optical surface which reflects nearly all light in the visible spectrum. There is some transmission in the region of 590 to 700 nanometers. Photopharmaceuticals are formulated to be activated by light energy in this region. Penetration depth is in the region of 1-3 mm from the dry corneocyte surface. It has been discovered that the interposition of a flexible transparent hydrogel coupling layer between a monochromatic plate or sheet-formed light source and the skin surface constitutes a new and more efficient delivery of activating optical energy to target dermal lesions for photodynamic therapy, particularly where the monochromatic light source delivers light at the specific wavelength at which the photopharmaceutical is photoactivated.

[0013] There are other substantial benefits that attend the use of an intimately contactive hydrogel coupling layer. Because hydrogels are typically 60 to 90% water, hydration of the stratum corneum occurs rapidly following contact with the hydrogel sheet. This hydration has a substantial optical transparency, or optical transmissiveness, enhancing effect, allowing more light to pass through the stratum corneum. Although the mechanism of this optical transparency has not been extensively studied, it is thought to result from a reduction of the light reflectivity of the stratum corneum through softening of the corneocytes by a solvent or plasticizing action. Castable transparent hydrogels are known in the art which may be cast into intimate physical and optical contact with, for example, a source of light.

[0014] This invention provides a composition for photodynamic therapy which comprises a photopharmaceutical in a shapeable water-containing hydrogel which is transparent to light used for said photodynamic therapy.

[0015] It is well established in the literature of chemical transport through the skin that hydration can enhance the chemical transparency, transmissiveness, passage or transport of pharmaceuticals through the stratum corneum. A review and discussion of this enhanced transport under hydrated conditions is found in Ghosh *et al., Pharmaceutical Tech.,* April 1993,

[0016] It follows that there are two key requirements of PDT to dermal structures where the protocol requires topical application of the photopharmaceutical: (1) transport of the photopharmaceutical into target tissue, and (2) subsequent light activation of the photopharmaceutical at the target tissue. These can be more efficiently accomplished using the diffusion route for both the drug and the activation optical energy.

[0017] A transparent hydrogel coupling layer thus serves the dual purposes of establishing conditions for optical energy diffusion into skin tissue and photopharmaceutical compound diffusion or other introduction into skin tissue, by intercellular or transcellular routes. It will be understood that the introduction of the photopharmaceutical from the hydrogel into the hydrated skin or through the hydrated stratum corneum, depending on the specific photopharmaceutical used, can be by the above-discussed diffusion, or by absorption, or by another mechanism constituting chemical permeation or penetration of the hydrated skin or stratum corneum. Another optical advantage of a transparent transport hydrogel is that it can remain in place after PDT exposure, as a protective dressing.

[0018] In a preferred embodiment of this invention, a transparent hydrogel serves as a transport or reservoir of a hydration agent and a photopharmaceutical and the hydrogel rapidly releases the photopharmaceutical to the skin tissue. For purposes of PDT, rapid delivery is desirable. This contrasts with prior art transdermal devices for non-PDT drug delivery which provide much slower release kinetics for system absorption. Further, in the present invention, the PDT is localized to a dermal treatment site defined by a cover, container or patch covering the site where the dermal lesion is located and the light necessary to activate the photopharmaceutical is delivered only to the dermal treatment site. The invention thus rapidly delivers the light activatable photopharmaceutical doses to skin tissue, and to a dermal lesion, and then delivers the light dose to initiate its biological activity to treat the dermal lesion.

[0019] The intimate transparent hydrogel contact established at the skin surface of the treatment site forms both a fluid or fluidic coupling for the photopharmaceutical and an optical or optic coupling for the photoactivating light. The hydrogel fills in discontinuities in the skin to reduce reflection and matches indices of refraction of the skin tissue. The water contained in the hydrogel matrix begins to solubilize the stratum corneum, hydrating this normally dry layer, and forms an avenue of exchange between the hydrogel and the dermal lesion. Hydration enhances both intracellular and transcellular pathways. Upon establishment of these pathways, transport of the photopharmaceutical to target tissue or dermal lesion commences.

[0020] The effect of hydration on fluid transport across the stratum corneum layer is substantial. Normally, this structure contains 10 to 15% water. Hydrated stratum corneum can retain up to 50% water and the normal light diffusion coefficient of the hydrated stratum corneum can increase ten-fold.

[0021] The effect of hydration on optical coupling of light into skin tissue is also substantial, but is sustaina-

ble only with the contact of the transparent hydrogel to both the skin tissue and the light source. In a preferred embodiment, a fiber optic panel comprising a plurality of fiber optic strands is used as a light delivery source to activate the photopharmaceutical, and hydrogel in contact with the fiber optic strands is efficient because at manufacture the hydrogel is cast against, and placed in intimate physical contact with, the fiber optic strands and conforms to the geometry of these strands, achieving intimate optical coupling. The formation of the hydrogel to skin surface juncture occurs at the point of engagement of the hydrogel-to-the-skin-surface. The physical characteristics of the hydrogel necessary to establish intimate skin contact are those described for electrode contact in the prior art references, cited above. Similar characteristics are required for performing PDT with the present invention, with the added hydrogel attributes of light transmission and hydration of the skin.

[0022] The mechanical changes hydration produces in the stratum corneum layer have a substantial impact on the optical coupling efficiency of externally applied light in the red region of the spectrum. The ultra-structure of the stratum corneum is an array of flattened essentially dead cells which are constantly being shed in a natural process of skin surface renewal. This results in a very uneven, dry, and highly light reflective layer or barrier to light penetration or transmission. Hydration by contact with emollients and oil-based unguents confers an improved surface but the effect is transitory under projected optical illumination schemes that, through surface heating, rapidly degrade the hydration effect by drying out the target region. Thus, though topically applied agents for PDT may briefly induce an optical improvement, it rarely persists through the projected light illumination phase if surface heating occurs during illumination.

[0023] This is in marked contrast to the present invention, where the hydrogel remains in place during the light dosage and serves as a hydration agent and photopharmaceutical reservoir or transport means, and a conduit and coupling for both light and fluidized agents to the target tissue or dermal treatment site during all phases of photodynamic therapy of a dermal lesion.

[0024] In one preferred embodiment, the invention includes a combination controller and patch for PDT of a dermal lesion located at a dermal treatment site on skin including the stratum corneum at the site. The controller is optically connected to the patch and the patch includes a transparent coupler (*e.g.,* hydrogel) for covering the dermal treatment site and which contains a hydration agent and, in some applications, a photopharmaceutical. The transparent coupler couples the hydration agent to the stratum corneum to hydrate and soften the stratum corneum to enhance its optical transmissiveness to facilitate the transmission of light therethrough and to enhance its chemical transmissiveness to facilitate the transmission therethrough of any photopharmaceutical to the dermal treatment site for treatment of the dermal lesion. A source of light delivery is included in the patch and receives optical energy from the controller and delivers the light through the transparent coupling and the hydrated stratum corneum to any photopharmaceutical at the site to photoactivate the photopharmaceutical to biologically engage and treat the dermal lesion. The invention permits the patient undergoing therapy to control and vary the applied therapy for the patient's comfort and to eliminate, or substantially eliminate, patient discomfort and even pain.

[0025] The invention also provides a method of applying PDT to a dermal lesion including the steps of hydrating the stratum corneum at the dermal treatment site to enhance its optical and chemical transparency or transmissiveness and introducing a photopharmaceutical and light through the hydrated stratum corneum to photoactivate the photopharmaceutical and cause it to biologically engage and treat the dermal lesion. In one preferred embodiment, the method of the present invention utilizes a transparent hydrogel containing a hydration agent and a photopharmaceutical to fluidically couple the photopharmaceutical to the hydrated stratum corneum and to optically couple the light to the hydrated stratum corneum to photoactivate the photopharmaceutical through the hydrated corneum to cause the photoactivated photopharmaceutical to biologically engage and treat the dermal lesions.

Brief Description of the Drawings

[0026]

FIG. 1 is a diagrammatical illustration, substantially in cross-section, illustrating prior art photodynamic therapy of a dermal lesion using projection optics;

FIG. 2 is a diagrammatical illustration, substantially in cross-section, illustrating a first embodiment of a patch of the present invention;

FIG. 2A is a partial cross-sectional view of the cover of a patch of the present invention and which illustrates that the internal surface of the cover may be provided with a suitable light reflecting layer or coating;

FIG. 3 is a perspective cut away diagrammatical illustration of a patch shown *in situ* over a dermal treatment site according to a first embodiment;

FIG. 3A is a partial perspective view of an optical fiber strand for illustrating diagrammatically the lateral, or radial, exiting of laser light;

FIG. 4 is an exploded view, partially in cross-section, illustrating a second embodiment of the present invention;

FIG. 5 is a perspective diagrammatical illustration, substantially in cross-section, illustrating the patch of the second embodiment shown *in situ* over a dermal treatment site and also showing connection to a laser diode;

FIG. 6 is a diagrammatical perspective view, partial-

ly in cross-section, illustrating a procedure tray containing the components of the first embodiment article of manufacture of the present invention illustrated in FIGS. 2 and 3;

FIG. 7 is a perspective view, in partial cutaway, illustrating an embodiment of the combination controller and patch of the present invention for applying photodynamic therapy to dermal lesions;

FIG. 8 is a general block diagram of a computer which can be included in the controller of the present invention and a general block diagram of a patch of the present invention;

FIG. 9 is a flow chart of a computer program stored in a programmed logic array which is executed without patient, or attending physician or clinician, intervention; and

FIG. 10 is a flow chart of another computer prcgram also stored in the programmed logic array which is executed with patient, or attending physician or clinician, intervention.

Detailed Description of Preferred Embodiments

[0027] FIG. 1 illustrates prior art PDT of dermal lesions 10 located in a person's skin indicated by general numerical designation 12, which skin includes the stratum corneum 14. It will be understood that the dermal lesions 10 are illustrated diagrammatically in FIG. 1, and in FIGS. 2, 3 and 5 referred to below, by the darkest spots shown in the skin 12. It will be further understood that the dermal lesions 10 are generally located under the stratum corneum 14 or within the skin 12 or can extend partly outwardly from the skin, as illustrated in FIG. 1.

[0028] Projective light source 13 directs light, indicated by arrows 16, onto the skin 12 and, as noted generally above, the stratum corneum 14 scatters the light with substantial portions of the light, as indicated by arrow 17, being reflected away from the stratum corneum 14 and thereby not initiating any photodynamic therapy. However, as further noted above, red light within the light 16 can penetrate the skin 12 to 3-4 mm. The projective light source 13 is typically either a filtered incandescent light source or a laser and is normally arranged to project the light 16 perpendicular to the skin 12 and corneum 14. It will be further understood from FIG. 1 that the dermal treatment site, indicated generally by numerical designation 18, is generally not well defined in distinction to the dermal treatment site produced by the present invention, to be described below and illustrated in FIG. 2.

[0029] Referring to FIG. 2, a first embodiment of a patch of the present invention, particularly useful in conjunction with the controller 72 of the present invention shown in FIG. 7 and described below, is indicated by general numerical designation 20. Patch 20 includes a cover 22, which may also be referred to as a container, and can be made, for example, of Mylar and suitably formed into the shape shown by, for example, vacuum forming. It will be noted that the lower portion of the cover 22 may be provided with an outwardly extending flange or peripheral portion 23 circumscribing the lower cover portion, and the peripheral portion 23 can be provided with a suitable layer of adhesive 24, of a type known in the art and which is compatible with human skin, for sealingly engaging the skin 12 to seal the cover 22 to the skin and define and cover a dermal treatment site indicated by general numerical designation 25. The flange or peripheral portion 23 and adhesive layer 24 are better seen in FIG. 2A. It will be noted that in use of the patch 20 of the present invention illustrated in FIG. 2, the dermal treatment site 25 is comparatively narrowly and well defined as contrasted to the open and comparatively poorly defined prior art dermal treatment site 18 illustrated in FIG. 1.

[0030] The cover 22 provides an internal chamber 22A, better seen in FIG. 2A, opposite the dermal treatment site 25 and a body or layer of transparent hydrogel 26 is received and resides within the chamber 22A. Transparent hydrogel 26 can be a transparent hydrogel of the type described above and can be, for example, a polyvinyl alcohol having a water matrix in which water serves as a hydration agent in the present invention. The water or hydration agent is illustrated diagrammatically in FIG. 2 by circles 27. In addition to containing the water or hydration agent 27, the transparent hydrogel 26 includes a suitable photopharmaceutical for treating the dermal lesions 10. This photopharmaceutical is illustrated diagrammatically in FIG. 2 by the circles 28. The photopharmaceutical 28 can be introduced into the transparent hydrogel 26 by absorption. The photopharmaceutical 28 can be, for example, photopharmaceutical 5-ALA available from the Sigma Chemical Company, St. Louis, Missouri, which is made photoactive by red light at a wavelength of substantially 635 nm. Suitable hydrogels are Aqutrix Lot R926C by Hydromer Inc. (Somerville, NJ, USA) and HYB0336 by Nepera Hydrogels (Harrison, NY, USA). Such gels can be shaped into a desired shape.

[0031] The patch 20, in FIG. 2, further includes a light delivery source indicated by general numerical designation 30 and which can be an optic laser light-emitting panel available from Lasermax, Inc., of Rochester, New York, which emits monochromatic red light having a wavelength of substantially 635 nm so as to be photoactively compatible with and matched to the photoactive wavelength of the photopharmaceutical 28 contained in the transparent hydrogel 26. The optic laser light-emitting panel 30 includes a plurality of optical fiber strands 31 indicated in transverse cross-section by the linearly aligned circles shown in FIG. 2 and which strands 31 may be better seen in the perspective view of FIG. 3.

[0032] Referring to FIG. 2A, the cover 22 includes an internal surface 34 which can be provided with a suitable layer or coating of reflective material 35 which can be a layer of suitable reflective foil adhered to the internal

surface 34, or thermally staked thereto, or can be a suitable reflective coating provided by a suitable deposition process. Reflective layer 35 is not shown in FIG. 2 because it is relatively thin as compared to the cover 22 but it will be understood that such reflective layer is present in patch 20 of FIG. 2. The optic laser light-emitting panel 30 resides within the chamber 22A and may be suitably secured to the cover 22, and to or through the reflective layer 35, by a suitable adhesive or by suitable thermal staking. In this embodiment, the transparent hydrogel 26 is a castable hydrogel and is cast into intimate physical and optical contact with the panel 30.

[0033] Referring to FIG. 3, it will be understood that the strands of optical fibers 31 of the optic laser light-emitting panel 30 are actually the ends or end portions of the optical fibers contained in the optical fiber bundle 36 which terminate in a suitable optical fiber connector 37. As shown in FIG. 4, the cover 22 is provided with a suitably sized opening 57 for admitting the optical fiber bundle 36 therethrough. Connector 37 is for being connected to a suitable laser diode 40 for producing, in one embodiment, monochromatic red light indicated by the arrows 42 having a wavelength of substantially 635 nm. The laser diode 40 can be, for example, a TOLD 635 available from Toshiba Optical Systems. The laser light 42 is transmitted or ducted to the optical strands 31, through the optical bundle 36 and, as may be understood from FIG. 3A, the optical fiber strands 31 are provided with side openings or lateral notches 39 which cause or permit the laser light 42 (FIG. 3) to be emitted at a number of angles from the sides of the strands 31 which is ultimately reflected by the reflective layer or surface 35 (FIG. 2A) and caused to be impinged upon the stratum corneum 14 and skin 12. As may be noted from FIG. 2, the laser light, as indicated by the arrows 29, is reflected off the reflective surface 35 (FIG. 2A) and is transmitted through the transparent hydrogel 26.

[0034] When the patch 20, FIGS. 2 and 3, is sealingly engaged to the skin 12 and stratum corneum 14 as illustrated in FIGS. 2 and 3 and as described above, the water or hydration agent 27 contained in the transparent hydrogel 26 engages the stratum corneum 14 and immediately begins to hydrate and soften the stratum corneum to enhance its optical transparency or transmissiveness to facilitate the transmission of the laser light therethrough and to enhance its chemical transparency or transmissiveness to facilitate the transmission therethrough of the photopharmaceutical 28 and into the dermal treatment site 25 containing the dermal lesions 10. The laser light 42 (FIG. 3) is introduced into the dermal treatment site 25 and illuminates the site by light diffusion which photoactivates the photopharmaceutical 28 to initiate its biological activity and to cause the photoactivated photopharmaceutical to biologically engage and treat the dermal lesion 10. After such treatment, as noted generally above, the cover 22 of the patch 20 may remain in place after the photodynamic therapy as a temporary protective dressing for the dermal treatment site 25. It will be further understood that, in this embodiment, a biologically sufficient quantity of photopharmaceutical is introduced into the hydrogel to accomplish treatment of the dermal lesion.

[0035] Referring now to FIGS. 4 and 5, a second embodiment of a patch of the present invention, particularly useful in combination with the controller 72 of the present invention shown in FIG. 7 and described below, is shown and indicated by general numerical designation 20A. The structural elements in patch 20A which are the same, or substantially the same, as the corresponding structural elements in patch 20 of FIGS. 2 and 3, are given the same numerical designation as the elements in FIGS. 2 and 3. It will be generally understood that patch 20A applies photodynamic therapy to dermal lesions 10, in FIG. 5, in substantially the same manner as patch 20 of FIGS. 2 and 3. However, in the embodiment 20A, the transparent hydrogel 26A includes the water or hydrating agent indicated by circles 27 in FIG. 2, but does not contain the photopharmaceutical indicated by circles 28 in FIG. 2. Patch 20A includes a second layer or sheet of transparent hydrogel 50 which is smaller in size and/or thickness than transparent hydrogel 26A and which, although containing a water matrix in which the photopharmaceutical is contained, is highly dehydrated as compared to the transparent hydrogel 26A. The relatively highly dehydrated state of the transparent hydrogel 50 permits the transparent hydrogel 50 to be cut and trimmed, such as by a pair of scissors 51, into a body of hydrogel 54 having a size much smaller than the transparent hydrogel 26A and shaped into substantially the same shape as the underlying dermal lesion(s) 10, in FIG. 5.

[0036] The photopharmaceutical contained in the transparent hydrogel 50 is toxic, typically acidic, and its application to the skin of a patient can be at least somewhat discomforting or even painful. By reducing the size of the hydrogel containing the photopharmaceutical, according to the invention, a reduced but still biologically sufficient quantity of photopharmaceutical can be applied photodynamically to the patient but with reduced discomfort. This also facilitates a photopharmaceutical profile that minimizes the application of the photopharmaceutical to healthy tissue at the dermal treatment site 25, in FIG. 5, yet allows the controlled delivery of photoactivating light to the entire dermal treatment site 25. In application, and in practice of the photodynamic therapy, the trimmed hydrogel 54 resides within the cover 22 intermediate with the transparent hydrogel 26A and the treatment site 25 as may be noted particularly from FIG. 5. The transparent hydrogel 26A and trimmed hydrogel body 54 function in basically the same manner as the single layer of transparent hydrogel 26 in patch 20 of FIGS. 2 and 3 to apply photodynamic therapy to the dermal lesion(s) 10.

[0037] A procedure tray is indicated by general numerical designation 60. Procedure tray 60 is a single use procedure tray and may be suitably thermoformed from

a suitable plastic such as polypropylene. It will be further understood that the patches 20 and 20A of the present invention are single use patches. The tray is compartmentalized, as shown, to receive, for example, the components or elements comprising the article of manufacture 20 shown in FIGS. 2 and 3. The transparent hydrogel 26 may be received within a moisture impervious foil or laminate pouch 61, the cover 22 and optic laser light-emitting panel 30 may be received in compartments as also shown. The procedure tray 60 is sealed against moisture variation by a "peelable" foil sealing panel 63. The sealing panel 63 is removed and the elements or components of the article of manufacture 20 are assembled as illustrated in FIGS. 2 and 3 and thereafter may be applied to the skin as described above and illustrated diagrammatically in FIGS. 2 and 3.

[0038] Referring now to FIG. 7, a combination controller and patch for applying photodynamic therapy to a dermal lesion embodying the present invention is shown with the combination being indicated by general numerical designation 70. Combination 70 includes controller 72 and patch 20 shown in FIGS. 2 and 3 and described above, or in the alternative patch 20A shown in FIGS. 4 and 5 and described above. It will be understood that the controller 72 and patch 20, or 20A, are of a size and weight such that they can be conveniently carried by a patient receiving the photodynamic therapy. The controller 72 can be provided with a suitable loop 73 through which a patient's belt may be inserted, or the controller 72 can be provided with a suitable clip (not shown) for clipping the controller to the patient's clothing.

[0039] Controller 72 includes a housing 74 which may be made of a suitable plastic suitably shaped into the configuration shown. Mounted to the housing 74 is a source of optical energy 75 which may be, for example, a solid state diode laser of the type noted above and which, in one embodiment, emits monochromatic red light having a wavelength of substantially 635 nm. Suitable collimating optics, or lens, 76 are mounted to the housing intermediate the diode laser 75 and the patch connector 37 for aligning and directing the optical energy or laser light 77, sometimes referred to as light flux, into the connector 37 and thereby into the bundle of optic fibers 36 and to and out the sides of the optical fiber strands 31 of the panel 30 as described above. It will be understood that the connector 37, as shown in FIGS. 3 and 5 and described above, is disconnectable from the housing 74, and it will be further understood that in a preferred embodiment of the present invention the patch 20 is a single use patch which may be disposed of after use. It will be further understood that the controller 72 is not disposable but instead may be used numerous times with different disposable patches. A power supply 78, which may be a plurality of suitable batteries such as rechargeable batteries, is mounted to the housing 74 to provide power to the solid state laser diode 75 and to a computer or processor indicated by general numerical designation 80.

[0040] Computer 80 is suitably mounted in the housing, such as by surface mounting technology of the type known in the art, and includes the microprocessor and clock 82 and programmed logic array 84 illustrated in block diagram form in FIG. 8. These components may be any one of several suitable components known in the art. The power supply 78 also provides power to the computer 80. A suitable liquid crystal display 85, in FIG. 7, is suitably mounted to the housing 74 and is connected operably to the microprocessor 82 as indicated diagrammatically in FIG. 8. It will be understood generally that the display 85 provides a visible indication to a patient undergoing PDT, or to an attending clinician or physician, of the treatment steps of the PDT that is being performed or its status. Generally, the patient, attending physician or clinician, operates the controller 72 to apply PDT to the patient's dermal lesion through depression of the power-on button 88. If desired, or required, a photodetector 93, may be mounted on the computer 80 and one or more optical fibers from the bundle 36 may be connected to the photodetector 93 whereby the optical energy or laser light applied to the optical fiber strands 31 can be sampled or monitored and suitable input provided from the photodetector 93 to the computer to provide further control of the optical energy or laser light applied to the patch 20 for photodynamic therapy as described above.

[0041] Control of the PDT applied to a dermal lesion can be by the patient receiving the PDT or by the attending clinician or physician and, more particularly, therapy is applied generally in accordance with the PDT dosage to be applied to the dermal treatment site pursuant to a preprogrammed time and intensity profile coded into the computer 80 and more particularly as coded into the programmed logic array 84, in FIG. 8, pursuant to the computer program flow charts set forth in FIGS. 9 and 10. The flow charts set forth in FIGS. 9 and 10 enable a computer programmer of ordinary skill in the art to write and introduce a program into the programmed logic array 84, in any one of several different computer programming languages, to cause the combination controller and patch of the present invention to apply PDT to treat a dermal lesion in accordance with the programmed instructions.

[0042] As noted above, photodynamic therapy applied to a dermal lesion can cause discomfort and even pain to the patient. As noted above with regard to the publications of Van Gemert *et al.* and Anderson *et al.*, PDT can be varied by varying the intensity and/or duration of optical energy or light applied to photoactivate the photopharmaceutical.

[0043] Referring again to FIG. 7, it will be noted that the controller 72 includes the above-noted power-on button 88, and a start button 89, a power level up button 90 and a power level down button 91. These buttons are also shown in FIG. 8 as being connected to the microprocessor and clock 82 of the computer 80. Upon the power-on button 88 being depressed, by the patient or

an attending physician or clinician, the controller 72 under the control of the computer 80, and pursuant to the program stored in the programmed logic array 84 in accordance with the flow chart set forth in FIG. 9, applies photodynamic therapy to a patient's dermal lesion as described above with regard to patches 20 and 20A. This program runs automatically in accordance with the dosimetry programmed into the computer in accordance with the predetermined photodynamic treatment protocol determined by the program instructions in the programmed logic array 84. If the patient experiences discomfort or pain during the automatic treatment protocol, the patient (or attending physician or clinician) can intervene by depressing the start button 89, which causes computer 80 to apply therapy according to FIG. 10. Unlike FIG. 9, the procedure of FIG. 10 allows the patient (or attending physician or clinician) to interactively control treatment parameters.

[0044] In the procedure shown in FIG. 10, if the patient experiences discomfort, the patient (or attending physician or clinician) can depress the power level down button 91 to decrease the intensity and/or duration of the optical energy or laser light being applied thereby decreasing the photoactivity of the photopharmaceutical and decreasing the patient's discomfort. If the patient is not experiencing discomfort and desires to accelerate the photodynamic therapy of the dermal lesion, the patient (or attending physician or clinician) can depress the power level up button 90 whereupon the computer 80, under the control of the programmed logic array 84 and the instructions programmed therein pursuant to FIG. 10, increases the intensity of the optical energy, or laser light, applied to the photopharmaceutical to increase its photoactivity until the patient again experiences discomfort whereupon the patient (or attending physician or clinician) can again depress the power level down button to reduce such discomfort.

[0045] It will be understood that the term photopharmaceutical as used herein and in the appended claims means an agent which is itself a photosensitizer or which is converted to a photosensitizer in the body.

[0046] Many variations and modifications of the above embodiments will occur to those skilled in the art. For example, optical sources and wavelength(s) other than those discussed above can be used in the invention. In addition, the invention can be used in applications other than those described above, for example, the invention can be used for hair removal.

Claims

1. An apparatus for photodynamic therapy of tissue, the apparatus comprising a source of light for irradiating said tissue with activating light and a fluid in intimate physical contact with said source of light and with the location of said tissue exposed to said light,

   characterised in that said fluid is a shapeable hydrogel which is transparent to said activating light.

2. An apparatus according to claim 1, wherein said hydrogel includes a photopharmaceutical.

3. An apparatus according to claim 1, wherein said hydrogel is in intimate contact with said source of light.

4. An apparatus according to claim 1, wherein said source of light emits monochromatic light.

5. An apparatus according to claim 1, wherein said source of light is a fiber optic panel.

6. An apparatus according to claim 5, wherein said fiber optic panel is connected to receive light from a laser diode via an optical fiber bundle.

7. An apparatus according to claim 1 for applying photodynamic therapy to a dermal lesion located at a dermal treatment site on the skin including the stratum corneum, comprising:

   a controller and patch for applying photodynamic therapy to the dermal lesion and including said hydrogel containing hydration agent, a photo-pharmaceutical and a light delivery unit;
   the controller including said source of light connected to said light delivery unit;
   said patch for being secured to said skin over the dermal treatment site to cause said transparent hydrogel to engage the stratum corneum to cause said hydration agent to hydrate the stratum corneum to enhance its chemical transparency to permit the photopharmaceutical to pass therethrough and enter the dermal treatment site and to enhance the optical transparency of the stratum corneum to facilitate the passage therethrough of light; and
   wherein said light delivery unit delivers said light through said transparent hydrogel and said hydrated stratum corneum to said photopharmaceutical at the dermal treatment site to photoactivate said photopharmaceutical to cause said photopharmaceutical to biologically engage and treat the dermal lesion.

8. An apparatus according to claim 7, wherein said patch includes a cover provided with a seal for sealing said cover over the dermal treatment site to cover the dermal treatment site, wherein said transparent hydrogel includes a water matrix providing said hydration agent and wherein said photopharmaceutical is absorbed into said water matrix.

9. An apparatus according to claim 8, wherein said

cover includes an internal surface defining a chamber for receiving said transparent hydrogel and wherein said transparent hydrogel resides in said chamber, and wherein said cover further comprises a reflective layer provided on said internal surface for reflecting said light through said transparent hydrogel and to said dermal treatment site.

10. An apparatus according to claim 8, wherein said source of light is a laser providing laser light, and wherein said light delivery unit comprises an array of optical fibers for emitting laser light from sides thereof, and wherein said cover is provided with an internal reflective surface for reflecting said laser light through said transparent hydrogel and said hydrated stratum corneum into the dermal treatment site, and wherein said transparent hydrogel comprises castable transparent hydrogel, and wherein said transparent hydrogel is cast into intimate physical and optical engagement with said array of optical fibers.

11. An apparatus according to claim 8, wherein said seal comprises a layer of adhesive applied to a peripheral portion of said cover for sealingly engaging the skin to seal said cover to the skin over the dermal treatment site.

12. An apparatus according to claim 7, wherein said transparent hydrogel comprises a first layer of hydrogel in said patch, and a second layer of hydrogel in said patch residing intermediate said first layer of hydrogel and the dermal treatment site, said first layer of hydrogel including a water matrix providing said hydration agent and said second layer of hydrogel being smaller in size than said first layer and generally shaped to cover substantially only a dermal lesion located at the dermal treatment site, said second layer of hydrogel including a water matrix into which said photopharmaceutical is absorbed.

13. An apparatus according to claim 7, wherein said controller includes a power supply for providing power to said source of light, and wherein said controller includes a computer for control by a patient receiving the photodynamic therapy, said computer connected to said power supply to permit said patient to control the amount of power supplied to said source of light and the time said power supply supplies power to said source of light to thereby permit the patient to control and vary the photodynamic therapy applied to the dermal lesion.

14. An apparatus according to claim 1 for photodynamic therapy of a dermal lesion located at a dermal treatment site on skin which includes the stratum corneum, comprising:

a cover which seals to the skin for covering and defining a dermal treatment site and for providing a chamber opposite the dermal treatment site;

said hydrogel containing hydration agent and at least one photopharmaceutical, said hydrogel residing in said chamber and for engaging the skin at the dermal treatment site to cause said hydration agent to hydrate the stratum corneum at the dermal treatment site to enhance the passage therethrough of light and said photopharmaceutical; and

a light delivery unit mounted to and inside of said cover and residing in said chamber for photoactivating said photopharmaceutical at said dermal treatment site to cause said photopharmaceutical to treat the dermal lesion.

15. An apparatus according to claim 14, wherein said transparent hydrogel includes a water matrix comprising said hydration agent.

16. An apparatus according to claim 14, wherein said light delivery unit comprises a fiber optic laser light-emitting panel having a plurality of optical fibers provided with side openings for the lateral transmission of laser light therethrough to photoactivate said photopharmaceutical.

17. An apparatus according to claim 16, wherein said cover includes an internal surface defining said chamber and wherein said cover further comprises a reflective layer provided on said internal surface for reflecting said laser light through said transparent hydrogel.

18. An apparatus according to claim 10 or 17, wherein said photopharmaceutical is photoactivatable at a predetermined wavelength and wherein said fiber optic provides monochromatic light at said predetermined wavelength.

19. An apparatus according to claim 18, wherein said predetermined wavelength is 635 nm.

20. An apparatus according to claim 14, wherein said cover includes a lower portion having an outwardly extending peripheral portion and a layer of adhesive applied to said peripheral portion for sealingly engaging the skin to seal said cover to the skin over said dermal treatment site.

21. An apparatus according to claim 14, wherein said hydrogel comprises a first layer of transparent hydrogel received in said chamber and a second layer of transparent hydrogel received in said chamber and residing intermediate said first layer of hydrogel and the dermal treatment site, said first layer of hy-

drogel including a water matrix providing said hydration agent and said second layer of hydrogel being smaller in size than said first layer and shaped to cover substantially only the dermal lesion located at the dermal treatment site, and said second layer of hydrogel including a water matrix into which said photopharmaceutical is absorbed.

22. An apparatus according to claim 1 for photodynamic therapy of a dermal lesion located at a dermal treatment site on skin which includes the stratum corneum, comprising:

a cover which seals to the skin for covering and defining a dermal treatment site and for providing a chamber opposite the dermal treatment site;
said hydrogel contained in said chamber and for covering the dermal treatment site, said transparent hydrogel containing at least one hydration agent and at least one photopharmaceutical, said hydrogel for coupling said hydration agent to the stratum corneum at the dermal treatment site to hydrate and soften the stratum corneum to enhance the optical transmissiveness of the stratum corneum to facilitate the transmission of light therethrough and to enhance its chemical transmissiveness to facilitate the transmission therethrough of said photopharmaceutical for treatment of the dermal lesion; and
a light delivery unit mounted to and inside said cover for delivering light through said transparent hydrogel and through the hydrated stratum corneum to illuminate the dermal treatment site by light diffusion to photoactivate said photopharmaceutical at said dermal treatment site to treat the dermal lesion.

23. A shapeable hydrogel for use in photodynamic therapy of tissue, the hydrogel being transparent to light used in said photodynamic therapy.

24. A composition for photodynamic therapy which comprises a photopharmaceutical in a shapeable water-containing hydrogel which is transparent to light used for said photodynamic therapy.

Patentansprüche

1. Vorrichtung zur photodynamischen Gewebetherapie mit einer Lichtquelle zum Bestrahlen des Gewebes mit Aktivierungslicht und einem Fluid in engem physischen Kontakt mit der Lichtquelle und der dem Licht ausgesetzten Gewebestelle,

dadurch gekennzeichnet, daß das Fluid in einem formbaren Hydrogel besteht, das für das Aktivierungslicht transparent ist.

2. Vorrichtung nach Anspruch 1, wobei das Hydrogel ein Photo-Arzneimittel aufweist.

3. Vorrichtung nach Anspruch 1, wobei das Hydrogel engen Kontakt mit der Lichtquelle hat.

4. Vorrichtung nach Anspruch 1, wobei die Lichtquelle monochromatisches Licht emittiert.

5. Vorrichtung nach Anspruch 1, wobei die Lichtquelle in einem optischen Faserfeld besteht.

6. Vorrichtung nach Anspruch 5, wobei das optische Faserfeld zum Empfangen von Licht von einer Laserdiode über ein optisches Faserbündel angeschlossen ist.

7. Vorrichtung nach Anspruch 1 zum Anwenden photodynamischer Therapie auf eine Hautschädigung an einer Haut-Eingriffsstelle auf der Haut einschließlich der Hornschicht, mit einer Steuereinheit und einem Flecken zum Anwenden der photodynamischen Therapie auf die Hautschädigung und mit dem Hydrationsmittel enthaltenden Hydrogel, einem Photo-Arzneimittel und einer Lichtfördereinheit, wobei

die Steuereinheit die Lichtquelle aufweist, die an die Lichtfördereinheit angeschlossen ist,

der Flecken zum Anbringen auf der Haut über der Haut-Eingriffsstelle ausgelegt ist, um das transparente Hydrogel in die Hornschicht eindringen zu lassen, um das Hydrationsmittel zur Hydration der Hornschicht zur Verbesserung ihrer chemischen Transparenz zu veranlassen, um dem Photo-Arzneimittel den Durchtritt und das Eintreten in die Haut-Eingriffsstelle zu ermöglichen und die optische Transparenz der Hornschicht zu steigern, um den Durchtritt von Licht dadurch zu erleichtern, und

die Lichtfördereinheit das Licht durch das transparente Hydrogel und die hydratisierte Hornschicht zu dem Photo-Arzneimittel an der Haut-Eingriffsstelle befördert, um das Photo-Arzneimttel zu photo-aktivieren und damit zum biologischen Einwirken und Behandeln der Hautschädigung zu veranlassen.

8. Vorrichtung nach Anspruch 7, wobei der Flecken eine Abdeckung aufweist, die mit einer Dichtung zum Dichten der Abdeckung über der Haut-Eingriffsstelle ausgestattet ist, um die Haut-Eingriffsstelle abzudecken, wobei das transparente Hydrogel eine Wassermatrix zum Bereitstellen des Hydrationsmittels aufweist, und wobei das Photo-Arzneimittel in die Wassermatrix absorbiert ist.

9. Vorrichtung nach Anspruch 8, wobei die Abdeckung

eine eine Kammer zur Aufnahme des transparenten Hydrogels definierende Innenfläche aufweist, und das transparente Hydrogel in der Kammer angesiedelt ist, und wobei die Abdeckung ferner auf der Innenfläche eine Reflexionsschicht zum Reflektieren des Lichts durch das transparente Hydrogel und zu der Haut-Eingriffsstelle aufweist.

10. Vorrichtung nach Anspruch 8, wobei die Lichtquelle in einem Laserlicht ausgebenden Laser besteht, die Lichtfördereinheit ein optisches Faser-Array zur Emission von Laserlicht von Stellen davon aufweist, die Abdeckung mit einer Reflexionsinnenfläche zum Reflektieren des Laserlichts durch das transparente Hydrogel und die hydratisierte Hornschicht in die Haut-Eingriffsstelle ausgestattet ist, das transparente Hydrogel formbares transparentes Hydrogel aufweist, und das transparente Hydrogel in engen physischen und optischen Eingriff mit dem optischen Faser-Array gebracht ist.

11. Vorrichtung nach Anspruch 8, wobei die Dichtung eine Klebstoffschicht aufweist, die auf einen Umfangsbereich der Abdeckung zum dichtenden Eingriff mit der Haut angebracht ist, um die Abdeckung in dichtenden Kontakt zu der Haut über der Haut-Eingriffsstelle zu bringen.

12. Vorrichtung nach Anspruch 7, wobei das transparente Hydrogel eine erste Hydrogel-Schicht in dem Flecken und eine zweite Hydrogel-Schicht in dem Flecken zwischen der ersten Schicht und der Haut-Eingriffsstelle aufweist, wobei die erste Hydrogel-Schicht eine Wassermatrix mit dem Hydrationsmittel aufweist, und die zweite Hydrogel-Schicht kleiner ist als die erste Schicht, und generell so geformt ist, daß sie im wesentlichen nur die Hautschädigung an der Haut-Eingriffsstelle abdeckt, wobei die zweite Hydrogel-Schicht eine Wassermatrix aufweist, in die das Photo-Arnzeimittel absorbiert ist.

13. Vorrichtung nach Anspruch 7, wobei die Steuereinheit eine Leistungsquelle zur Energieversorgung der Lichtquelle aufweist, die Steuereinheit einen Computer zur Steuerung durch einen die photodynamische Therapie empfangenden Patienten aufweist, und der Computer an die Leistungsquelle angeschlossen ist, um dem Patienten die Steuerung des der Lichtquelle zugeführten Energiebetrags und der Zeit, über die die Leistungsquelle Leistung zu der Lichtquelle zuführt, erlaubt, um dem Patienten damit zu ermöglichen, die auf die Hautschädigung angewandte photodynamische Therapie zu steuern und zu variieren.

14. Vorrichtung nach Anspruch 1 zur photodynamischen Therapie einer an einer Haut-Eingriffsstelle auf der Haut einschließlich der Hornschicht befindlichen Hautschädigung, mit:

einer Abdeckung mit dichtendem Kontakt zur Haut zum Abdecken und Definieren einer Haut-Eingriffsstelle, und zum Bereitstellen einer Kammer gegenüber der Haut-Eingriffsstelle;
dem Hydrogel, das ein Hydrationsmittel und wenigstens ein Photo-Arzneimittel enthält, in der Kammer angesiedelt ist und zum Eindringen in die Haut an der Haut-Eingriffsstelle ausgelegt ist, um das Hydrationsmittel zur Hydration der Hornschicht an der Haut-Eingriffsstelle zu veranlassen, um den Durchtritt von Licht und Photo-Arzneimttel dadurch zu steigern; und
einer Lichtfördereinheit, die innerhalb der Abdeckung angebracht und innerhalb der Kammer angesiedelt ist, zum Photo-Aktivieren des Photo-Arzneimittels an der Haut-Eingriffsstelle, um die Behandlung der Hautschädigung durch das Photo-Arzneimittel auszulösen.

15. Vorrichtung nach Anspruch 14, wobei das transparente Hydrogel eine Wassermatrix mit dem Hydrationsmittel aufweist.

16. Vorrichtung nach Anspruch 14, wobei die Lichtfördereinheit ein optisches, Laserlicht emittierendes Faserfeld mit mehreren optischen Fasern aufweist, die mit Seitenöffnungen zur lateralen Transmission von Laserlicht dadurch versehen sind, um das Photo-Arzneimittel zu photo-aktivieren.

17. Vorrichtung nach Anspruch 16, wobei die Abdekkung eine die Kammer definierende Innenfläche aufweist, und die Abdeckung ferner auf der Innenfläche eine Reflexionsschicht zum Reflektieren des Laserlichts durch das transparente Hydrogel aufweist.

18. Vorrichtung nach Anspruch 10 oder 17, wobei das Photo-Arzneimittel bei einer vorbestimmten Wellenlänge photo-aktivierbar ist, und die Faseroptik monochromatisches Licht bei dieser vorbestimmten Wellenlänge liefert.

19. Vorrichtung nach Anspruch 18, wobei die vorbestimmte Wellenlänge bei 635 nm liegt.

20. Vorrichtung nach Anspruch 14, wobei die Abdekkung einen unteren Bereich mit einem nach außen verlaufenden Umfangsbereich und eine auf den Umfangsbereich angebrachte Klebstoffschicht zum dichtenden Eingriff mit der Haut aufweist, um die Abdeckung dichtend mit der Haut über der Haut-Eingriffsstelle zu verbinden.

21. Vorrichtung nach Anspruch 14, wobei das Hydrogel eine erste transparente Hydrogelschicht in der

Kammer und eine zweite transparente Hydrogelschicht in der Kammer zwischen der ersten Hydrogelschicht und der Haut-Eingriffsstelle aufweist, die erste Hydrogelschicht eine Wassermatrix mit dem Hydrationsmittel aufweist, und die zweite Hydrogelschicht kleiner ist als die erste Schicht und so geformt, daß sie im wesentlichen nur die an der Haut-Eingriffsstelle befindliche Hautschädigung abdeckt, und die zweite Hydrogelschicht eine Wassermatrix aufweist, in die das Photo-Arzneimittel absorbiert ist.

22. Vorrichtung nach Anspruch 1 zur photodynamischen Therapie einer Hautschädigung, die sich auf einer Haut-Eingriffsstelle auf Haut mit Hornschicht befindet, mit:

einer dichtend mit der Haut verbundenen Abdeckung zum Abdecken und Definieren einer Haut-Eingriffsstelle und zum Bereitstellen einer Kammer gegenüber der Haut-Eingriffsstelle;
dem in der Kammer enthaltenen Hydrogel zum Abdecken der Haut-Eingriffsstelle, wobei das transparente Hydrogel wenigstens ein Hydrationsmittel und wenigstens ein Photo-Arzneimittel aufweist, zum Ansetzen des Hydrationsmittels an die Hornschicht an der Haut-Eingriffsstelle, um die Hornschicht zu hydratisieren und weich zu machen, um die optische Transparenz der Hornschicht zu steigern, um die Lichttransmission dadurch zu erleichtern, und um seine chemische Transparenz zu steigern, um die Transmission des Photo-Arzneimittels zur Behandlung der Hautschädigung dadurch zu erleichtern; und
einer Lichtfördereinheit, die innerhalb der Abdeckung zur Lichtförderung durch das transparente Hydrogel und durch die hydratisierte Hornschicht angebracht ist, um die Haut-Eingriffsstelle durch Lichtdiffusion zu beleuchten, um das Photo-Arzneimttel an der Haut-Eingriffsstelle zu photo-aktivieren, um die Hautschädigung zu behandeln.

23. Formbares Hydrogel zur Verwendung in der photodynamischen Gewebetherapie, das für das in der photodynamischen Therapie verwendete Licht transparent ist.

24. Zusammensetzung für photodynamische Therapie mit einem Photo-Arzneimittel in einem formbaren, Wasser enthaltenden Hydrogel, das für das in der photodynamischen Therapie verwendete Licht transparent ist.

Revendications

1. Dispositif de thérapie photodynamique de tissu, le dispositif comportant une source de lumière pour irradier ledit tissu à l'aide d'une lumière d'activation et un fluide en contact physique intime avec ladite source de lumière et avec l'emplacement dudit tissu exposé à ladite lumière,
caractérisé en ce que ledit fluide est un hydrogel modelable qui est transparent à ladite lumière d'activation.

2. Dispositif selon la revendication 1, dans lequel ledit hydrogel comporte un composé photo-pharmaceutique.

3. Dispositif selon la revendication 1, dans lequel ledit hydrogel est en contact intime avec ladite source de lumière.

4. Dispositif selon la revendication 1, dans laquelle ladite source de lumière émet une lumière monochromatique.

5. Dispositif selon la revendication 1, dans lequel ladite source de lumière est un panneau de fibres optiques.

6. Dispositif selon la revendication 5, dans lequel ledit panneau de fibres optiques est connecté pour recevoir une lumière provenant d'une diode laser via un faisceau de fibres optiques.

7. Dispositif selon la revendication 1 pour appliquer une thérapie photodynamique à une lésion dermique située au niveau d'un site de traitement dermique sur la peau incluant la couche cornée, comportant :

un contrôleur et un patch pour appliquer une thérapie photodynamique à la lésion dermique et incluant ledit hydrogel contenant un agent d'hydratation, un composé photo-pharmaceutique et une unité de diffusion de lumière,
le contrôleur incluant ladite source de lumière connectée à ladite unité de diffusion de lumière, ledit patch étant destiné à être fixé à ladite peau sur le site de traitement dermique pour amener ledit hydrogel transparent à venir en contact avec la couche cornée afin d'amener ledit agent d'hydratation à hydrater la couche cornée afin d'augmenter sa transparence chimique pour permettre au composé photo-pharmaceutique de passer à travers et d'entrer dans le site de traitement dermique et d'accentuer la transparence optique de la couche cornée afin de faciliter le passage à travers celle-ci d'une lumière, et

dans lequel ladite unité de diffusion de lumière diffuse ladite lumière à travers ledit hydrogel transparent et ladite couche cornée hydratée dans ledit composé pharmaceutique au niveau du site de traitement dermique pour photoactiver ledit composé photo-pharmaceutique afin d'amener ledit composé photo-pharmaceutique à venir au contact avec et à traiter biologiquement la lésion dermique.

8. Dispositif selon la revendication 7, dans lequel ledit patch comporte un couvercle muni d'un joint étanche pour sceller ledit couvercle sur le site de traitement dermique afin de recouvrir le site de traitement dermique, dans lequel ledit hydrogel transparent comporte une matrice d'eau fournissant ledit agent d'hydratation et dans lequel ledit composé photo-pharmaceutique est absorbé dans ladite matrice d'eau.

9. Dispositif selon la revendication 8, dans lequel ledit couvercle comporte une surface interne définissant une chambre pour recevoir ledit hydrogel transparent, ledit hydrogel transparent se trouvant dans ladite chambre, et dans lequel ledit couvercle comporte de plus une couche réflectrice agencée sur ladite surface interne pour réfléchir ladite lumière à travers ledit hydrogel transparent et dans ledit site de traitement dermique.

10. Dispositif selon la revendication 8, dans lequel ladite source de lumière est un laser délivrant une lumière laser, et dans lequel ladite unité de diffusion de lumière comporte un groupement de fibres optiques pour émettre une lumière laser depuis des côtés de celui-ci, et dans lequel ledit couvercle est muni d'une surface réflectrice interne pour réfléchir ladite lumière laser à travers ledit hydrogel transparent et ladite couche cornée hydratée dans le site de traitement dermique, et dans lequel ledit hydrogel transparent comporte un hydrogel transparent pouvant être coulé, et dans lequel ledit hydrogel transparent est coulé en contact physique et optique intime avec ledit groupement de fibres optiques.

11. Dispositif selon la revendication 8, dans lequel ledit joint étanche comporte une couche d'adhésif appliquée sur une partie périphérique dudit couvercle pour venir au contact de manière étanche de la peau afin de sceller ledit couvercle à la peau sur le site de traitement dermique.

12. Dispositif selon la revendication 7, dans lequel ledit hydrogel transparent comporte une première couche d'hydrogel dans ledit patch, une seconde couche d'hydrogel dans ledit patch se trouvant à une position intermédiaire entre ladite première couche d'hydrogel et le site de traitement dermique, ladite première couche d'hydrogel comportant une matrice d'eau fournissant ledit agent d'hydratation et ladite seconde couche d'hydrogel étant plus petite en termes de taille que ladite première couche et généralement formée pour recouvrir essentiellement uniquement une lésion dermique située au niveau du site de traitement dermique, ladite seconde couche d'hydrogel comportant une matrice d'eau dans laquelle ledit composé photo-pharmaceutique est absorbé.

13. Dispositif selon la revendication 7, dans lequel ledit contrôleur comporte une alimentation en courant pour délivrer un courant dans ladite source de lumière, et dans lequel ledit contrôleur comporte un ordinateur pour une commande par un patient recevant la thérapie photodynamique, ledit ordinateur étant connecté à ladite alimentation en courant pour permettre audit patient de commander la quantité de courant délivrée dans ladite source de lumière et la durée pendant laquelle ladite alimentation en courant délivre un courant dans ladite source de lumière de manière à permettre au patient de commander et de faire varier la thérapie photodynamique appliquée à la lésion dermique.

14. Dispositif selon la revendication 1 pour une thérapie photodynamique d'une lésion dermique située au niveau d'un site de traitement dermique sur la peau incluant la couche cornée, comportant :

un couvercle qui se scelle à la peau pour recouvrir et définir un site de traitement dermique et pour fournir une chambre en vis-à-vis du site de traitement dermique,
ledit hydrogel contenant un agent d'hydratation et au moins un composé photo-pharmaceutique, ledit hydrogel résidant dans ladite chambre et venant au contact de la peau au niveau du site de traitement dermique pour amener ledit agent d'hydratation à hydrater la couche cornée au niveau du site de traitement dermique afin d'augmenter le passage à travers celui-ci d'une lumière et dudit composé photo-pharmaceutique, et
une unité de diffusion de lumière montée sur ledit couvercle et à l'intérieur de celui-ci, et se trouvant dans ladite chambre pour photoactiver ledit composé photo-pharmaceutique au niveau dudit site de traitement dermique afin d'amener ledit composé photo-pharmaceutique à traiter la lésion dermique.

15. Dispositif selon la revendication 14, dans lequel ledit hydrogel transparent comporte une matrice d'eau comportant ledit agent d'hydratation.

16. Dispositif selon la revendication 14, dans lequel ladite unité de diffusion de lumière comporte un panneau d'émission de lumière laser à fibres optiques ayant une pluralité de fibres optiques munies d'ouvertures latérales pour la transmission latérale d'une lumière laser à travers celles-ci afin de photoactiver ledit composé photo-pharmaceutique.

17. Dispositif selon la revendication 16, dans lequel ledit couvercle comporte une surface interne définissant ladite chambre et dans lequel ledit couvercle comporte de plus une couche réflectrice agencée sur ladite surface interne pour réfléchir ladite lumière laser à travers ledit hydrogel transparent.

18. Dispositif selon la revendication 10 ou 17, dans lequel ledit composé photo-pharmaceutique peut être photoactivé à une longueur d'onde prédéterminée et dans lequel ladite fibre optique délivre une lumière monochromatique à ladite longueur d'onde prédéterminée.

19. Dispositif selon la revendication 18, dans lequel ladite longueur d'onde prédéterminée est de 635 nm.

20. Dispositif selon la revendication 14, dans lequel ledit couvercle comporte une partie inférieure ayant une partie périphérique s'étendant vers l'extérieur et une couche d'adhésif appliquée sur ladite partie périphérique pour venir au contact de manière étanche avec la peau afin de sceller ledit couvercle à la peau sur ledit site de traitement dermique.

21. Dispositif selon la revendication 14, dans lequel ledit hydrogel comporte une première couche d'hydrogel transparent reçue dans ladite chambre et une seconde couche d'hydrogel transparent reçue dans ladite chambre et se trouvant à un niveau intermédiaire entre ladite première couche d'hydrogel et le site de traitement dermique, ladite première couche d'hydrogel comportant une matrice d'eau fournissant ledit agent d'hydratation et ladite seconde couche d'hydrogel étant plus petite en termes de taille que ladite première couche et mise en forme pour recouvrir essentiellement uniquement la lésion dermique située au niveau du site de traitement dermique, et ladite seconde couche d'hydrogel comportant une matrice d'eau dans laquelle ledit composé photo-pharmaceutique est absorbé.

22. Dispositif selon la revendication 1 pour une thérapie photodynamique d'une lésion dermique située au niveau d'un site de traitement dermique sur la peau incluant la couche cornée, comportant :

un couvercle qui se Scelle sur la peau pour recouvrir et définir ainsi le traitement dermique et pour fournir une chambre en vis-à-vis du site de traitement dermique,
ledit hydrogel contenu dans ladite chambre et destiné à recouvrir le site de traitement dermique, ledit hydrogel transparent contenant au moins un agent d'hydratation et au moins un composé photo-pharmaceutique, ledit hydrogel étant destiné à coupler ledit agent d'hydratation et la couche cornée au niveau du site de traitement dermique pour hydrater et ramollir la couche cornée afin d'accentuer la capacité de transmission optique de la couche cornée afin de faciliter la transmission d'une lumière à travers celle-ci et pour augmenter sa capacité de transmission chimique pour faciliter la transmission à travers celle-ci dudit composé photo-pharmaceutique pour le traitement de la lésion dermique, et
une unité de diffusion de lumière montée sur ledit couvercle et à l'intérieur de celui-ci, pour diffuser une lumière à travers ledit hydrogel transparent et à travers ladite couche cornée hydratée afin d'illuminer le site de traitement dermique par une diffusion de lumière pour photoactiver ledit composé photo-pharmaceutique au niveau dudit site de traitement dermique afin de traiter la lésion dermique.

23. Hydrogel modelable destiné à être utilisé dans une thérapie photodynamique de tissu, l'hydrogel étant transparent à une lumière utilisée dans ladite thérapie photodynamique.

24. Composition pour une thérapie photodynamique qui comporte un composé photo-pharmaceutique dans un hydrogel modelable contenant de l'eau qui est transparent à une lumière utilisée pour ladite thérapie photodynamique.

FIG. 1
PRIOR ART

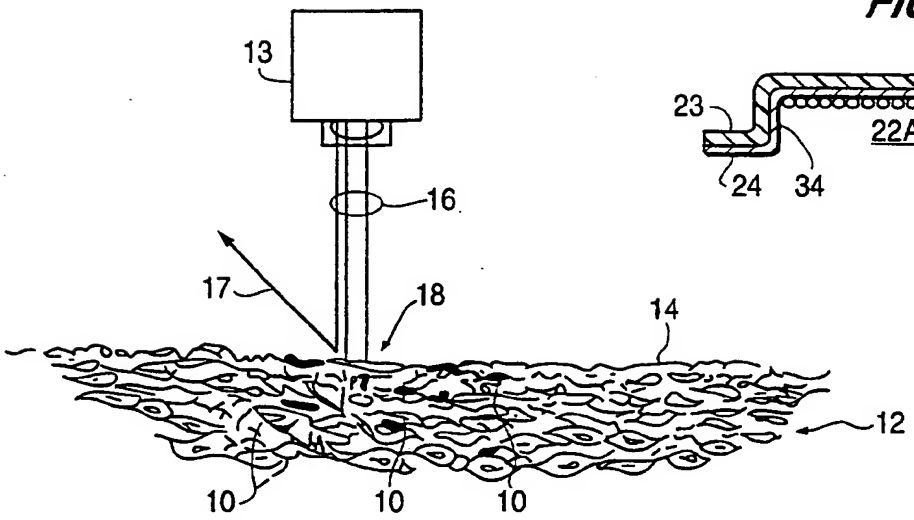


FIG. 2A

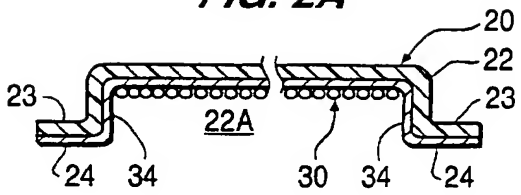


FIG. 2

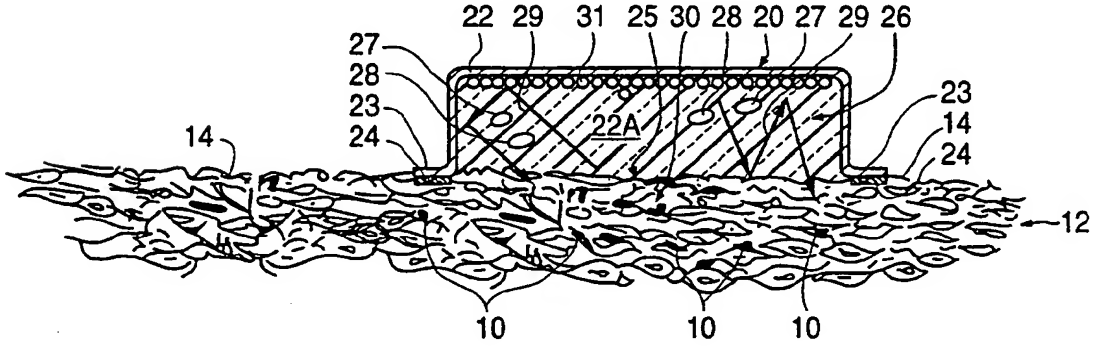


FIG. 3A

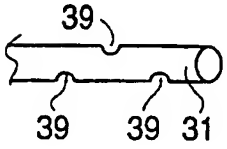
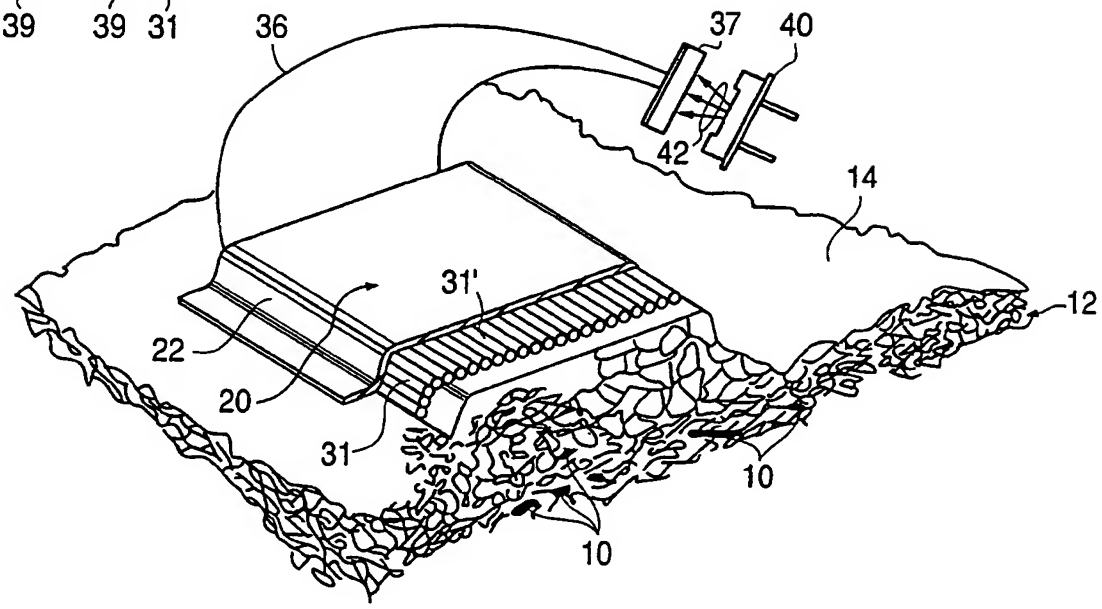


FIG. 3



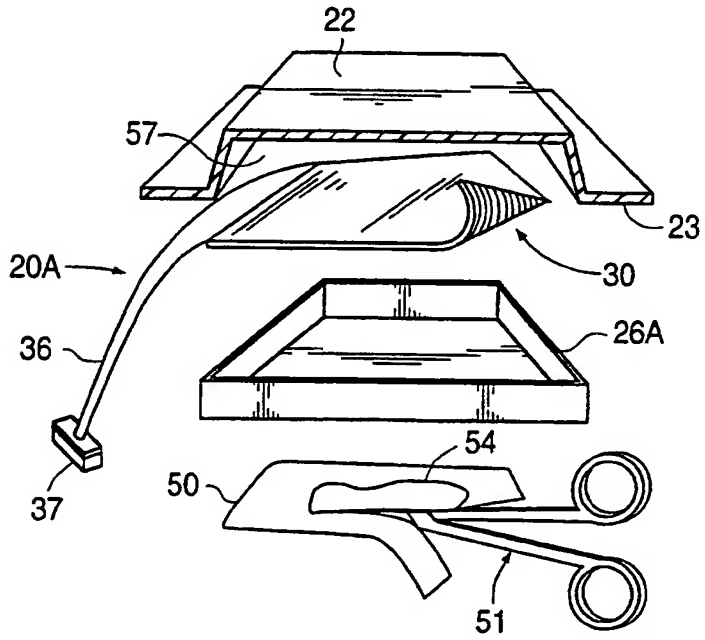


FIG. 4

FIG. 5

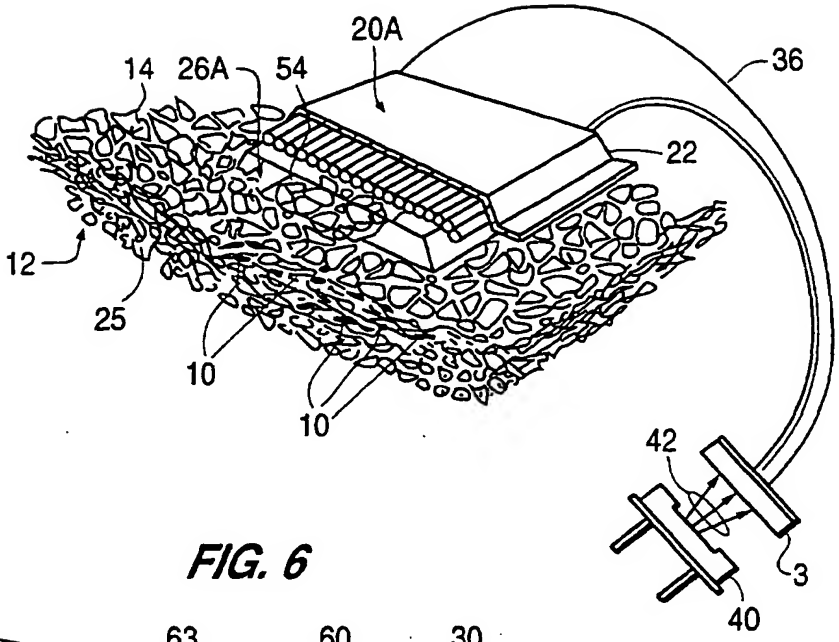


FIG. 6

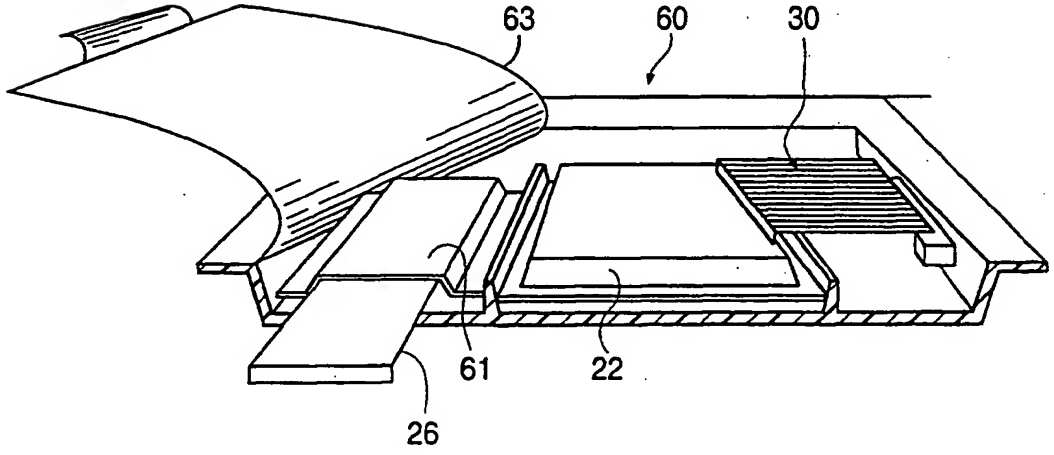


FIG. 7

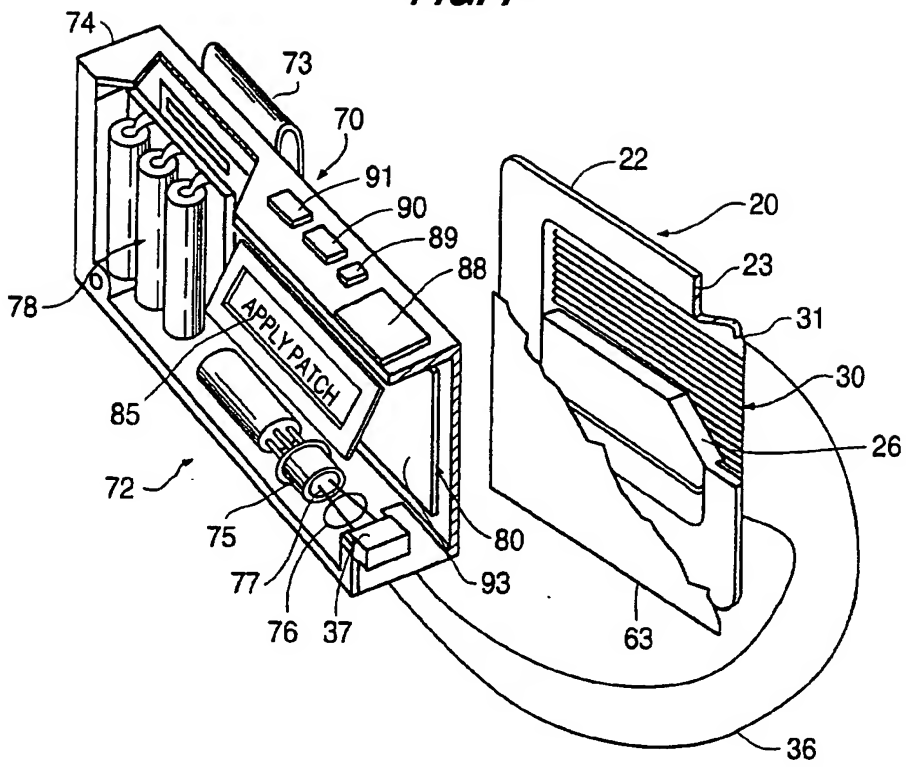

74
73
70
91
90
89
88
78
APPLY PATCH
85
72
75
77
76
37
80
93
22
20
23
31
30
26
63
36

FIG. 8

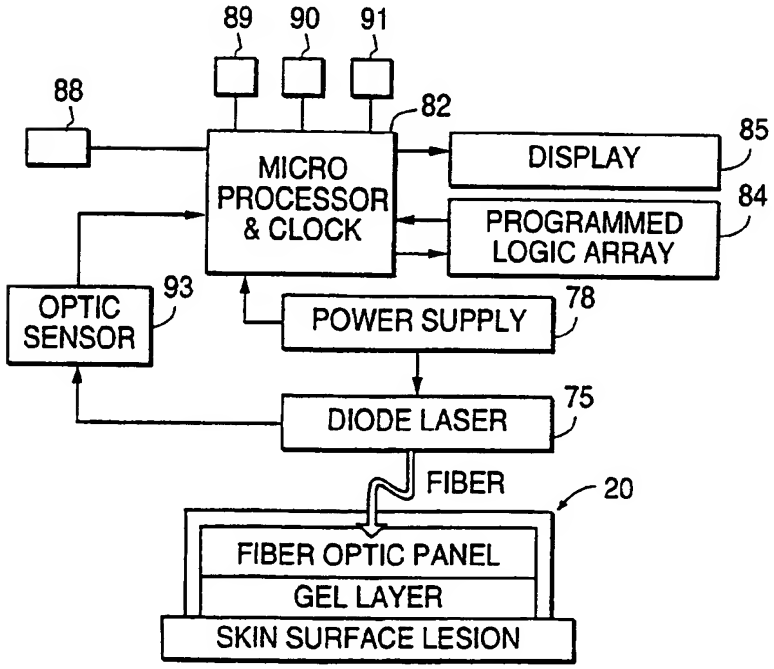

89
90
91
88
82
MICRO PROCESSOR & CLOCK
DISPLAY
85
PROGRAMMED LOGIC ARRAY
84
OPTIC SENSOR
93
POWER SUPPLY
78
DIODE LASER
75
FIBER
20
FIBER OPTIC PANEL
GEL LAYER
SKIN SURFACE LESION

FIG. 9

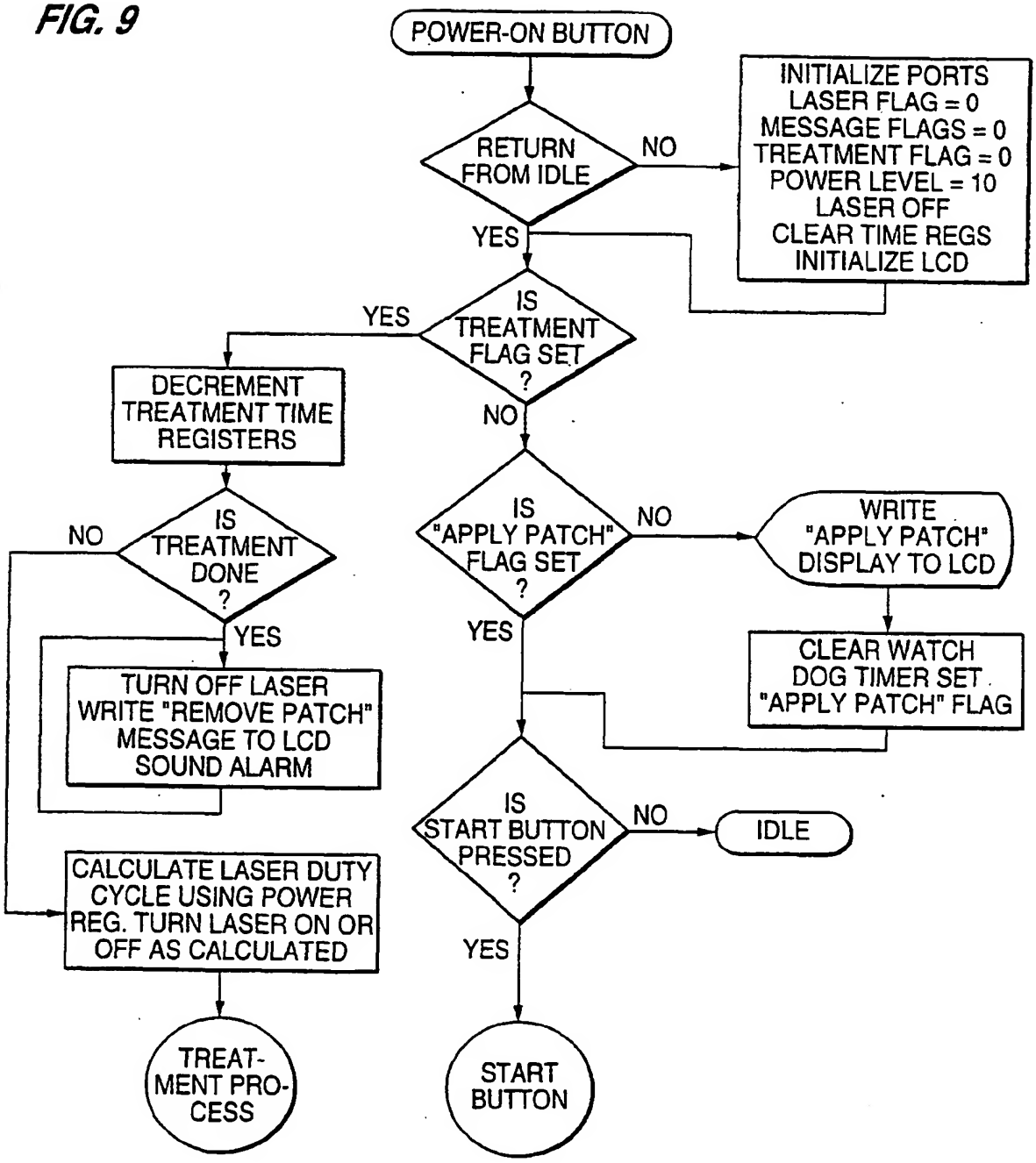
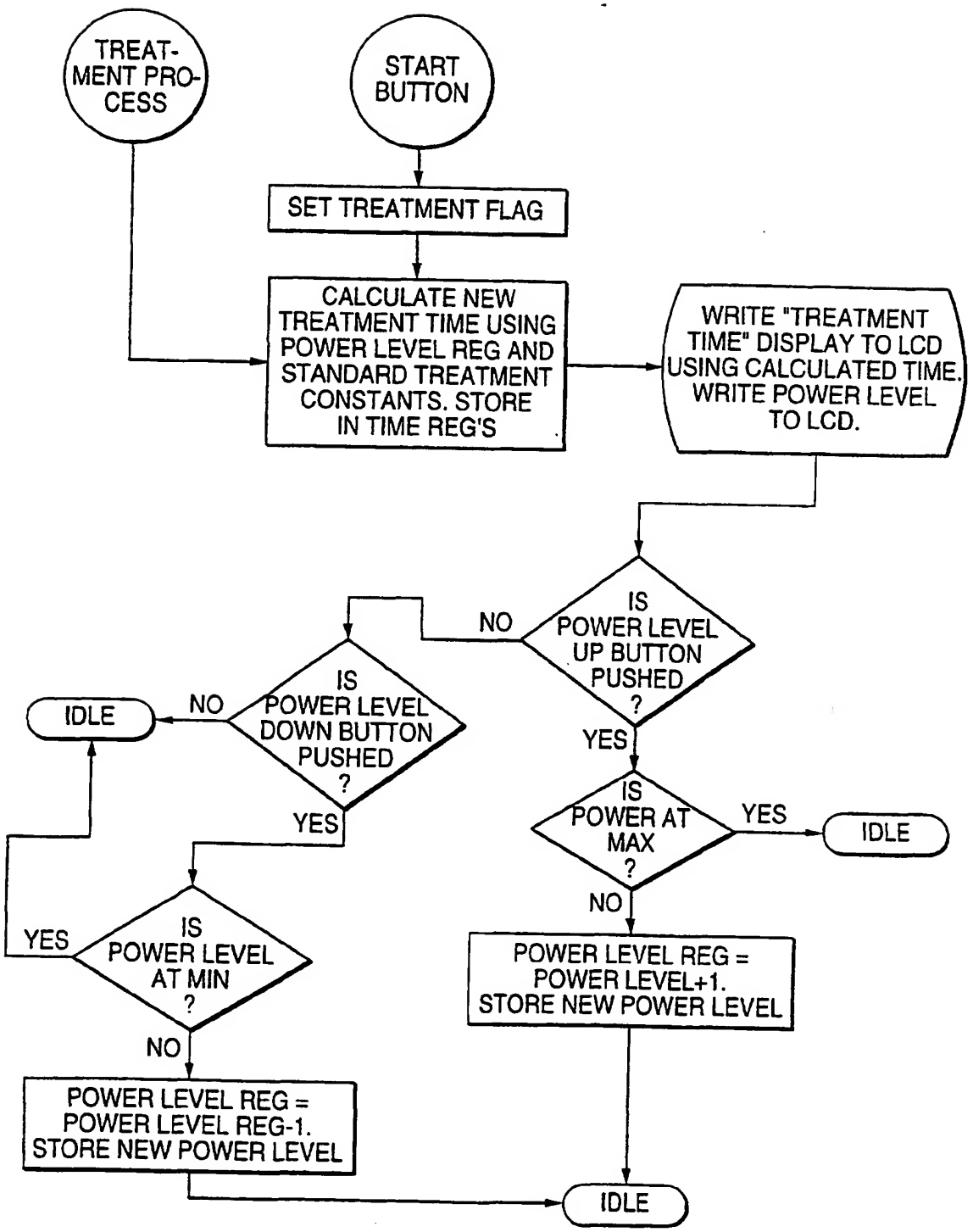

POWER-ON BUTTON
RETURN FROM IDLE
NO
INITIALIZE PORTS
LASER FLAG = 0
MESSAGE FLAGS = 0
TREATMENT FLAG = 0
POWER LEVEL = 10
LASER OFF
CLEAR TIME REGS
INITIALIZE LCD
YES
IS TREATMENT FLAG SET ?
YES
DECREMENT TREATMENT TIME REGISTERS
NO
IS TREATMENT DONE ?
NO
YES
TURN OFF LASER
WRITE "REMOVE PATCH" MESSAGE TO LCD
SOUND ALARM
CALCULATE LASER DUTY CYCLE USING POWER REG. TURN LASER ON OR OFF AS CALCULATED
TREAT-MENT PRO-CESS
IS "APPLY PATCH" FLAG SET ?
NO
WRITE "APPLY PATCH" DISPLAY TO LCD
YES
CLEAR WATCH DOG TIMER SET "APPLY PATCH" FLAG
IS START BUTTON PRESSED ?
NO
IDLE
YES
START BUTTON

FIG. 10


TREAT-
MENT PRO-
CESS
START
BUTTON
SET TREATMENT FLAG
CALCULATE NEW
TREATMENT TIME USING
POWER LEVEL REG AND
STANDARD TREATMENT
CONSTANTS. STORE
IN TIME REG'S
WRITE "TREATMENT
TIME" DISPLAY TO LCD
USING CALCULATED TIME.
WRITE POWER LEVEL
TO LCD.
IS
POWER LEVEL
UP BUTTON
PUSHED
?
NO
YES
IS
POWER AT
MAX
?
YES
IDLE
NO
POWER LEVEL REG =
POWER LEVEL+1.
STORE NEW POWER LEVEL
IS
POWER LEVEL
DOWN BUTTON
PUSHED
?
NO
IDLE
YES
IS
POWER LEVEL
AT MIN
?
YES
NO
POWER LEVEL REG =
POWER LEVEL REG-1.
STORE NEW POWER LEVEL
IDLE